INVENTOR SEARCH

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L10 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:316356 HCAPLUS Full-text
DOCUMENT NUMBER: 142:367666
TITLE: Compositions and methods using farnesoid X receptor agonists for treatment of fibrosis
INVENTOR(S): Liu, Yaping; Moore, John Tomlin
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Jones, Stacey Ann
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005032549 | A1 | 20050414 | WO 2004-US29748 | 20040910 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1696910 | A1 | 20060906 | EP 2004-783821 | 20040910 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| US 20070015796 | A1 | 20070118 | US 2006-572974 | 20060322 |
| PRIORITY APPLN. INFO.: | | | US 2003-506394P | P 20030926 |
| | | | WO 2004-US29748 | W 20040910 |

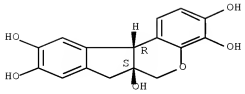
OTHER SOURCE(S): MARPAT 142:367666

AB Methods for the treatment of fibrosis, including liver fibrosis, via administration of FXR agonists are provided. FXR agonist GW4064 reduced collagen deposition in livers of rats treated with CCl4.

IC ICM A61K031-42
CC 1-7 (Pharmacology)
ST fibrosis treatment farnesoid X receptor agonist; GW4064 FXR agonist treatment liver fibrosis
IT Nuclear receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FXR (farnesoid X receptor), agonists; farnesoid X receptor agonists for treatment of fibrosis)
IT Cytoprotective agents
Mammalia
Prophylaxis
(farnesoid X receptor agonists for treatment of fibrosis)
IT Liver, disease
(fibrosis, treatment of; farnesoid X receptor agonists for treatment of fibrosis)
IT Fibrosis
(hepatic, treatment of; farnesoid X receptor agonists for treatment of

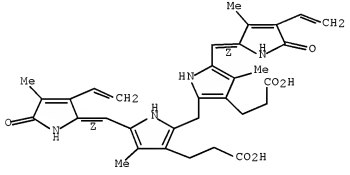
fibrosis)
IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(naturally occurring, FXR agonist administration with; farnesoid X receptor agonists for treatment of fibrosis)
IT Organic compounds, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic small, as FXR agonists; farnesoid X receptor agonists for treatment of fibrosis)
IT Fibrosis
(treatment of; farnesoid X receptor agonists for treatment of fibrosis)
IT Collagens, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(type I, GW4064 reduction of deposition of, in rats treated with carbon tetrachloride; farnesoid X receptor agonists for treatment of fibrosis)
IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β1-; farnesoid X receptor agonists for treatment of fibrosis)
IT 517-28-2 635-65-4 9000-86-6 9000-97-9
9001-60-9 9001-78-9 9002-02-2
9003-98-9 9046-27-9 17372-87-1
65666-07-1 192526-67-3
RL: PRPH (Prophetic)
(Compositions and methods using farnesoid X receptor agonists for treatment of fibrosis)
IT 278779-30-9, GW4064
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as farnesoid X receptor agonist; farnesoid X receptor agonists for treatment of fibrosis)
IT 140208-24-8, TIMP1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(farnesoid X receptor agonists for treatment of fibrosis)
IT 849654-17-7 849654-18-8 849654-19-9
849654-20-2 849654-21-3 849654-22-4
849654-23-5 849654-24-6 849654-25-7
849654-26-8 849654-27-9 849654-28-0
849654-29-1 849654-30-4 849654-31-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; compns. and methods using farnesoid X receptor agonists for treatment of fibrosis)
IT 517-28-2 635-65-4 9000-86-6 9000-97-9
9001-60-9 9001-78-9 9002-02-2
9003-98-9 9046-27-9 17372-87-1
65666-07-1 192526-67-3
RL: PRPH (Prophetic)
(Compositions and methods using farnesoid X receptor agonists for treatment of fibrosis)
RN 517-28-2 HCAPLUS
CN Benz[b]indeno[1,2-d]pyran-3,4,6a,9,10(6H)-pentol, 7,11b-dihydro-, (6aS,11bR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 635-65-4 HCAPLUS
CN 21H-Biline-8,12-dipropanoic acid, 2,17-diethenyl-1,10,19,22,23,24-hexahydro-3,7,13,18-tetramethyl-1,19-dioxo- (CA INDEX NAME)

Double bond geometry as shown.



RN 9000-86-6 HCAPLUS
CN Aminotransferase, alanine (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9000-97-9 HCAPLUS
CN Aminotransferase, aspartate (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-60-9 HCAPLUS
CN Dehydrogenase, lactate (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-78-9 HCAPLUS
CN Phosphatase, alkaline (CA INDEX NAME)

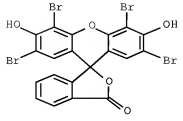
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9002-02-2 HCAPLUS
CN Dehydrogenase, succinate (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9003-98-9 HCAPLUS
CN Nuclease, deoxyribo- (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9046-27-9 HCAPLUS
CN Glutamyltransferase, γ- (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 17372-87-1 HCAPLUS
CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one,

2',4',5',7'-tetrabromo-3',6'-dihydroxy-, sodium salt (1:2) (CA INDEX NAME)



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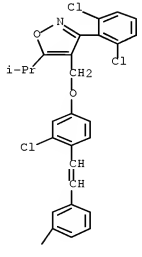
RN 65666-07-1 HCAPLUS
CN Silymarin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 192526-67-3 HCAPLUS
CN TRIzol (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 278779-30-9, GW4064
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as farnesoid X receptor agonist; farnesoid X receptor agonists for treatment of fibrosis)
RN 278779-30-9 HCAPLUS
CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



HO2C

IT 140208-24-8, TIMP1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(farnesoid X receptor agonists for treatment of fibrosis)
RN 140208-24-8 HCAPLUS
CN Proteinase inhibitor, TIMP 1 (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 849654-17-7 849654-18-8 849654-19-9
849654-20-2 849654-21-3 849654-22-4
849654-23-5 849654-24-6 849654-25-7
849654-26-8 849654-27-9 849654-28-0
849654-29-1 849654-30-4 849654-31-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; compns. and methods using farnesoid X receptor agonists for treatment of fibrosis)
RN 849654-17-7 HCAPLUS
CN DNA, d(T-C-C-T-G-A-C-C-C-T-G-A-A-G-T-A-T-C-C-G-A-T-A) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-18-8 HCAPLUS
CN DNA, d(G-G-T-G-C-C-A-G-A-T-C-T-T-T-T-C-C-A-T-G-T-C) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-19-9 HCAPLUS
CN DNA, d(A-A-C-A-C-G-G-C-A-T-C-A-T-C-A-C-C-A-A-C-T-G-G-G-A) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-20-2 HCAPLUS
CN DNA, d(T-T-C-A-C-C-T-A-C-A-G-C-A-C-G-C-T-T-G-T-G) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-21-3 HCAPLUS
CN DNA, d(G-A-T-G-A-C-T-G-T-C-T-T-G-C-C-C-C-A-A-G-T-T) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-22-4 HCAPLUS
CN DNA, d(A-T-G-G-C-T-G-C-A-C-G-A-G-T-C-A-C-A-C-C-G) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-23-5 HCAPLUS
CN DNA, d(C-C-A-A-A-G-C-C-A-C-C-G-G-A-G-T-C-T-T) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-24-6 HCAPLUS
CN DNA, d(G-C-T-T-G-A-A-G-C-C-A-A-T-C-C-T-T-G-G-A) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-25-7 HCAPLUS
CN DNA, d(C-T-C-T-G-C-G-C-T-C-C-A-T-T-C-C-A-C-C-T-T-A-T-A-A-C-A-C-C) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 849654-26-8 HCAPLUS
CN DNA, d(G-A-A-C-C-G-C-A-G-C-G-A-G-G-A-G-T-T-T) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-27-9 HCAPLUS
CN DNA, d(G-G-C-A-G-T-G-A-T-G-T-G-C-A-A-A-T-T-T-C-C) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-28-0 HCAPLUS
CN DNA, d(T-C-A-T-C-G-C-G-G-G-C-C-G-T-T-T-A-A-G-G-A-A) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-29-1 HCAPLUS
CN DNA, d(G-C-T-G-C-T-G-A-C-C-C-C-C-A-C-T-G-A-T) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-30-4 HCAPLUS
CN DNA, d(G-C-C-A-C-T-G-C-C-G-G-A-C-A-A-C-T-C) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 849654-31-5 HCAPLUS
CN DNA, d(C-G-C-C-T-G-A-G-T-G-G-C-T-G-T-C-T-T-T-T-G-A-C-G-T) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DISPLAY OF REQUESTED COMPOUND

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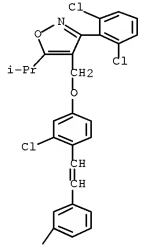
L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN 278779-30-9 REGISTRY
ED Entered STN: 20 Jul 2000
CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)
OTHER NAMES:
CN GW 4064
DR 292047-56-4
MF C28 H22 Cl3 N O4
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL

PAGE 1-A

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

56 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
56 REFERENCES IN FILE CAPLUS (1907 TO DATE)
ED Entered STN: 20 Jul 2000

RESULTS FROM SEARCHES IN REGISTRY, CAPLUS, USPATFULL, MEDLINE, BIOSIS, EMBASE, AND DRUGU

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=> d que stat l21
L11           1 SEA FILE=REGISTRY ABB=ON  278779-30-9/RN
L12          56 SEA FILE=HCAPLUS ABB=ON  L11
L17          46 SEA L12 AND ?LIVER?
L18          19 SEA L17 AND (PRD<20030926 OR PD<20030926)
L19           5 SEA L18
L20           5 DUP REMOV L19 (0 DUPLICATES REMOVED)
L21          22 DUP REMOV L18 L20 (2 DUPLICATES REMOVED)


=> d ibib abs hitstr l21 1-22

L21  ANSWER 1 OF 22  USPATFULL on STN
ACCESSION NUMBER:         2007:114810  USPATFULL  Full-text
TITLE:                    Combination therapy for the treatment of diabetes
INVENTOR(S):              Erondu, Ngozi E., Englishtown, NJ, UNITED STATES
                          Fong, Tung M., Somerset, NJ, UNITED STATES
                          Kanatani, Akio, Ushiku-shi, JAPAN
                          MacNeil, Douglas J., Westfield, NJ, UNITED STATES
                          Van Der Ploeg, Leonardus H.T., Lansdale, PA, UNITED
                          STATES

                               NUMBER        KIND    DATE
                          ---------------- ------ --------
PATENT INFORMATION:       US 20070099884     A1   20070503
APPLICATION INFO.:        US 2004-559206     A1   20040602  (10)
                          WO 2004-US17291          20040602
                                                   20051202  PCT 371 date

                                 NUMBER         DATE
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PRIORITY INFORMATION:     US 2003-476388P    20030606 (60)            <--
DOCUMENT TYPE:            Utility
FILE SEGMENT:             APPLICATION
LEGAL REPRESENTATIVE:     MERCK AND CO., INC, P O BOX 2000, RAHWAY, NJ,
                          07065-0907, US
NUMBER OF CLAIMS:         31
EXEMPLARY CLAIM:          1
LINE COUNT:               3437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB       The present invention relates to compositions comprising an anti-obesity
         agent and an anti-diabetic agent useful for the treatment of diabetes,
         diabetes associated with obesity and diabetes-related disorders. The present
         invention further relates to methods of treating or preventing obesity, and
         obesity-related disorders, in a subject in need thereof by administering a
         composition of the present invention. The present invention further provides
         for pharmaceutical compositions, medicaments, and kits useful in carrying
         out these methods.


CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT   278779-30-9, GW 4064
         (combination therapy of diabetes and diabetes-related disorders using
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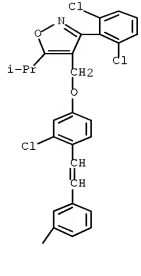
antiobesity agent and antidiabetic agent and other agents)
RN 278779-30-9 USPATFULL
CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A




PAGE 2-A




L21 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1124587 HCAPLUS Full-text
DOCUMENT NUMBER: 142:69188
TITLE: Combination therapy for the treatment of diabetes
INVENTOR(S): Erondu, Ngozi E.; Fong, Tung M.; MacNeil, Douglas J.; Van Der Ploeg, Leonardus H. T.; Kanatani, Akio
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004110375 | A2 | 20041223 | WO 2004-US17291 | 20040602 <-- |
| WO 2004110375 | A3 | 20050512 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1635832 A2 20060322 EP 2004-753999 20040602 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

US 20070099884 A1 20070503 US 2005-559206 20051202 <--

PRIORITY APPLN. INFO.: US 2003-476388P P 20030606 <--

WO 2004-US17291 W 20040602

OTHER SOURCE(S): MARPAT 142:69188

AB The present invention relates to compns. comprising an anti-obesity agent and an anti-diabetic agent useful for the treatment of diabetes, diabetes associated with obesity and diabetes-related disorders. The present invention further relates to methods of treating or preventing obesity, and obesity-related disorders, in a subject in need thereof by administering a composition of the present invention. The present invention further provides for pharmaceutical compns., medicaments, and kits useful in carrying out these methods.

IT 278779-30-9, GW 4064

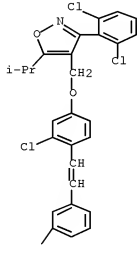
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination therapy of diabetes and diabetes-related disorders using antiobesity agent and antidiabetic agent and other agents)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A




PAGE 2-A

HO2C

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

L21 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1124581 HCAPLUS Full-text
DOCUMENT NUMBER: 142:69181
TITLE: Combination therapy for the treatment of hypertension
INVENTOR(S): Fong, Tung M.; Erondu, Ngozi E.; Macneil, Douglas J.; Mcintyre, James H.; Van Der Ploeg, Leonardus H. T.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004110368 | A2 | 20041223 | WO 2004-US17090 | 20040602 <-- |
| WO 2004110368 | A3 | 20060720 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
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| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| US 20060160834 | A1 | 20060720 | US 2005-559111 | 20051202 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-476390P | P 20030606 <-- |
| | | | WO 2004-US17090 | W 20040602 |

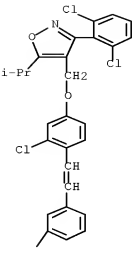
OTHER SOURCE(S): MARPAT 142:69181

AB The present invention relates to compns. comprising an anti-obesity agent and an anti-hypertensive agent useful for the treatment of hypertension, hypertension associated with obesity, and hypertension-related disorders. The present invention further relates to methods of treating or preventing obesity, and obesity-related disorders, in a subject in need thereof by administering a composition of the present invention. The present invention further provides for pharmaceutical compns., medicaments, and kits useful in carrying out these methods.

IT 278779-30-9, GW 4064
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy of hypertension and hypertension-related disorders using antiobesity agent and antihypertensive agent and other agents and antihypertensive agent)

RN 278779-30-9 HCAPLUS
CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:453343 HCAPLUS Full-text
DOCUMENT NUMBER: 141:19434
TITLE: Crystal structure of the human farnesoid X receptor ligand binding domain complexed with fexaramine and identification and development of novel small molecule ligands for FXR
INVENTOR(S): Downes, Michael R.; Verdicia, Mark A.; Noel, Joseph P.; Evans, Ronald M.; Bowman, Lindsey J.; Bowman, Marianne
PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004046323 | A2 | 20040603 | WO 2003-US36548 | 20031114 <-- |
| WO 2004046323 | A3 | 20041209 | | |

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|---|
| AU 2003298654 | A1 | 20040615 | AU 2003-298654 | | 20031114 | <-- |
| US 20060194949 | A1 | 20060831 | US 2005-535042 | | 20050513 | <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-426665P | P | 20021115 | <-- |
| | | | US 2002-426668P | P | 20021115 | <-- |
| | | | WO 2003-US36548 | W | 20031114 | |

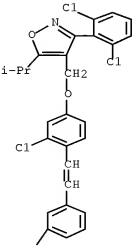
AB The present invention provides compns. comprising the ligand binding domain (LBD) of a human farnesoid X receptor (FXR) in crystalline form. In alternative embodiments, the LBD of FXR is complexed with a ligand therefor. There are provided high resolution structures and structure coordinates of FXR complexed with a novel high affinity agonist, fexaramine. The discovered structure of a FXR LBD provides the first three-dimensional view of the structural basis for FXR ligand binding. The present invention further provides a computer for producing a three-dimensional representation of FXR or a complex thereof, and a computer for determining at least a portion of the structure coordinates of FXR or a complex thereof. The present invention further provides methods of using this structural information to predict mols. capable of binding to FXR; to identify compds. with agonist, antagonist or partial agonist activity for FXR; and to determine whether a test compound is capable of binding to the LBD of FXR. The present invention further provides compns. comprising compds. identified by such invention methods. Identification and development of novel small mol. ligands for FXR, and activation of FXR and induction of FXR target genes by these novel compds. is disclosed.

IT 278779-30-9P, GW4064
RL: BSU (Biological study, unclassified); CPN (Combinatorial preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(FXR ligand; crystal structure of human farnesoid X receptor ligand binding domain complexed with fexaramine and identification and development of novel small mol. ligands for FXR)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



HO2C

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2004:151445 USPATFULL Full-text
TITLE: Method for identifying compounds modulating reverse cholesterol transport
INVENTOR(S): Staels, Bart, Petit Enghien, BELGIUM

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 20040115666 | A1 | 20040617 | |
| APPLICATION INFO.: | US 2003-450257 | A1 | 20031105 | (10) |
| | WO 2002-FR410 | | 20020204 | |

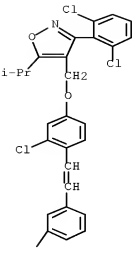
| | NUMBER | DATE | |
|---|---|---|---|
| PRIORITY INFORMATION: | FR 2001-1486 | 20010205 | <-- |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NIXON & VANDERHYE, PC, 1100 N GLEBE ROAD, 8TH FLOOR, ARLINGTON, VA, 22201-4714
NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1094
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention concerns methods and compounds capable of modulating reverse cholesterol transport in a mammal and screening methods for selecting, identifying and/or characterizing compounds capable of modulating reverse cholesterol transport. It also concerns cells, vectors and genetic constructs used for implementing said methods, and pharmaceutical compositions for treating atherosclerosis.

The methods of the invention are based on the use of FXR response elements derived from the apo A-I gene promoter.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 278779-30-9, GW 4064
(apoA1 promoter-derived FXR response element-based method for identifying compds. modulating reverse cholesterol transport)
RN 278779-30-9 USPATFULL
CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L21 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:777952 HCAPLUS Full-text
DOCUMENT NUMBER: 139:286360
TITLE: Methods using farnesoid X receptor (FXR) agonists for weight loss and alteration of cell metabolism
INVENTOR(S): Jones, Stacey Ann; Kliewer, Steven Anthony; Mansfield, Traci Ann
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Curagen Corporation
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003080803 | A2 | 20031002 | WO 2003-US8634 | 20030319 <-- |
| WO 2003080803 | A3 | 20041021 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| AU 2003225903 | A1 | 20031008 | AU 2003-225903 | | 20030319 <-- |
| US 20050107475 | A1 | 20050519 | US 2004-507082 | | 20040909 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-366463P | P | 20020321 <-- |
| | | | WO 2003-US8634 | W | 20030319 <-- |

OTHER SOURCE(S): MARPAT 139:286360

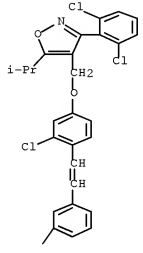
AB Treatment of human hepatocytes with farnesoid X receptor (FXR) agonists resulted in increased expression of FGF-19. Methods of using FXR agonists to alter cell metabolism, and in pharmaceutical weight loss methods, are described.

IT 278779-30-9, GW4064 278779-30-9D, GW4064, amino acid conjugates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesoid X receptor agonists for weight loss and alteration of cell metabolism)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

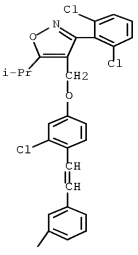



PAGE 2-A


RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:855658 HCAPLUS Full-text
DOCUMENT NUMBER: 139:317457
TITLE: Compositions and methods using farnesoid X receptor ligands for hepatoprotection and treatment of cholestasis
INVENTOR(S): Kliewer, Steven Anthony; Willson, Timothy Mark
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 20030203939 | A1 | 20031030 | US 2002-132311 | 20020425 |
| US 6987121 | B2 | 20060117 | | |
| WO 2003090745 | A1 | 20031106 | WO 2003-US10519 | 20030407 <-- |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003226283 A1 20031110 AU 2003-226283 20030407 <--
EP 1501506 A1 20050202 EP 2003-747270 20030407 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: US 2002-132311 A 20020425 <--
WO 2003-US10519 W 20030407 <--

OTHER SOURCE(S): MARPAT 139:317457

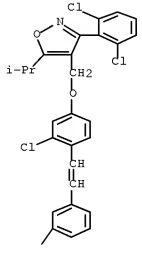
AB Methods for the treatment of cholestatic liver disease and reduction and prevention of hepatic injury resulting from cholestasis via administration of a FXR ligand are provided. Bile duct-ligated rats treated with FXR ligand GW4064 had a pronounced improvement in liver function as defined by a reduction in a panel of liver disease serum marker enzymes.

IT 278779-30-9, GW4064
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FXR agonist; farnesoid X receptor ligands for hepatoprotection and treatment of cholestasis)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A




PAGE 2-A

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REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:723027 HCAPLUS Full-text
DOCUMENT NUMBER: 139:286515

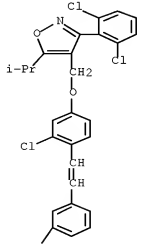
TITLE: Estrogen receptor α regulates expression of the orphan receptor small heterodimer partner
AUTHOR(S): Lai, KehDih; Harnish, Douglas C.; Evans, Mark J.
CORPORATE SOURCE: Wyeth Research, Collegeville, PA, 19426, USA
SOURCE: Journal of Biological Chemistry (2003), 278(38), 36418-36429
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hormonal status can influence diverse metabolic pathways. Small heterodimer partner (SHP) is an orphan nuclear receptor that can modulate the activity of several transcription factors. Estrogens are here shown to directly induce expression of the SHP in the mouse and rat liver and in human HepG2 cells. SHP is rapidly induced within 2 h following treatment of mice with ethynylestradiol (EE) or the estrogen receptor α (ERα)-selective compound Pr pyrazole triol (PPT). SHP induction by these estrogens is completely absent in ERαKO mice. Mutation of the human SHP promoter defined HNF-3, HNF-4, GATA, and AP-1 sites as important for basal activity, whereas EE induction required two distinct elements located between -309 and -267. One of these elements contains an estrogen response element half-site that bound purified ERα, and ERα with a mutated DNA binding domain was unable to stimulate SHP promoter activity. This ERα binding site overlaps the known farnesoid X receptor (FXR) binding site in the SHP promoter, and the combination of EE plus FXR agonists did not produce an additive induction of SHP expression in mice. Surprisingly, induction of SHP by EE did not inhibit expression of the known SHP target genes cholesterol 7α-hydroxylase (CYP7A1) or sterol 12α-hydroxylase (CYP8B1). However, the direct regulation of SHP expression may provide a basis for some of the numerous biol. effects of estrogens.

IT 278779-30-9, GW4064
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(estrogen receptor α regulates expression of orphan receptor small heterodimer partner as studied in mouse and rat liver and in human HepG2 cells)

RN 278779-30-9 HCAPLUS
CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



HO2C

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:579493 HCAPLUS Full-text
DOCUMENT NUMBER: 139:256039
TITLE: Human kininogen gene is transactivated by the farnesoid X receptor
AUTHOR(S): Zhao, Annie; Lew, Jane-L.; Huang, Li; Yu, Jinghua; Zhang, Theresa; Hrywna, Yaroslav; Thompson, John R.; de Pedro, Nuria; Blevins, Richard A.; Pelaez, Fernando; Wright, Samuel D.; Cui, Jisong
CORPORATE SOURCE: Departments of Atherosclerosis and Endocrinology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Biological Chemistry (2003), 278(31), 28765-28770
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

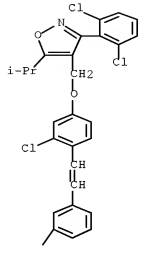
AB Human kininogen belongs to the plasma kallikrein-kinin system. High mol. weight kininogen is the precursor for two-chain kinin-free kininogen and bradykinin. It has been shown that the two-chain kinin-free kininogen has the properties of anti-adhesion, anti-platelet aggregation, and anti-thrombosis, whereas bradykinin is a potent vasodilator and mediator of inflammation. In this study the human kininogen gene is strongly up-regulated by agonists of the farnesoid X receptor (FXR), a nuclear receptor for bile acids. In primary human hepatocytes, both the endogenous FXR agonist chenodeoxycholate and synthetic FXR agonist GW4064 increased kininogen mRNA with a maximum induction of 8-10-fold. A more robust induction of kininogen expression was observed in HepG2 cells, where kininogen mRNA was increased by chenodeoxycholate or GW4064 up to 130-140-fold as shown by real time PCR. Northern blot anal. confirmed the up-regulation of kininogen expression by FXR agonists. To determine whether kininogen is a direct target of FXR, the authors examined the sequence of the kininogen promoter and identified a highly conserved FXR response element (inverted repeat, IR-1) in the proximity of the kininogen promoter (-66/-54). FXR/RXRα heterodimers specifically bind to this IR-1. A construct of a minimal promoter with the luciferase reporter containing this IR-1 was transactivated by FXR. Deletion or mutation of this IR-1 abolished FXR-mediated promoter activation, indicating that this IR-1 element is responsible for the promoter transactivation by FXR. The authors conclude that kininogen is a novel and direct target of FXR, and bile acids may play a role in the vasodilation and anti-coagulation processes.

IT 278779-30-9, GW4064
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(human kininogen gene is transactivated by the farnesoid X receptor in primary human hepatocytes)

RN 278779-30-9 HCAPLUS
CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-

4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:973413 HCAPLUS Full-text
DOCUMENT NUMBER: 140:229012
TITLE: Hepatoprotection by the farnesoid X receptor agonist GW4064 in rat models of intra- and extrahepatic cholestasis
AUTHOR(S): Liu, Yaping; Binz, Jane; Numerick, Mary Jo; Dennis, Steve; Luo, Guizhen; Desai, Bhasha; MacKenzie, Kathleen I.; Mansfield, Traci A.; Kliewer, Steven A.; Goodwin, Bryan; Jones, Stacey A.
CORPORATE SOURCE: Nuclear Receptor Functional Analysis, High Throughput Biology, GlaxoSmithKline, Research Triangle Park, NC, USA
SOURCE: Journal of Clinical Investigation (2003), 112(11), 1678-1687
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Farnesoid X receptor (FXR) is a bile acid-activated transcription factor that is a member of the nuclear hormone receptor superfamily. Fxr-null mice exhibit a phenotype similar to Byler disease, an inherited cholestatic liver disorder. In the liver, activation of FXR induces transcription of transporter genes involved in promoting bile acid clearance and represses genes involved in bile acid biosynthesis. We investigated whether the

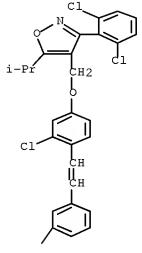
synthetic FXR agonist GW4064 could protect against cholestatic liver damage in rat models of extrahepatic and intrahepatic cholestasis. In the bile duct-ligation and α-naphthylisothiocyanate models of cholestasis, GW4064 treatment resulted in significant redns. in serum alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase, as well as other markers of liver damage. Rats that received GW4064 treatment also had decreased incidence and extent of necrosis, decreased inflammatory cell infiltration, and decreased bile duct proliferation. Anal. of gene expression in livers from GW4064-treated cholestatic rats revealed decreased expression of bile acid biosynthetic genes and increased expression of genes involved in bile acid transport, including the phospholipid flippase MDR2. The hepatoprotection seen in these animal models by the synthetic FXR agonist suggests FXR agonists may be useful in the treatment of cholestatic liver disease.

IT 278779-30-9, GW4064
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatoprotection by farnesoid X receptor agonist GW4064 in rat models of intra- and extrahepatic cholestasis)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:698404 HCAPLUS Full-text
DOCUMENT NUMBER: 140:87450
TITLE: Farnesoid X receptor agonists suppress hepatic

apolipoprotein CIII expression

AUTHOR(S): Claudel, Thierry; Inoue, Yusuke; Barbier, Olivier; Duran-Sandoval, Daniel; Kosykh, Vladimir; Fruchart, Jamila; Fruchart, Jean-Charles; Gonzalez, Frank J.; Staels, Bart

CORPORATE SOURCE: Departement d'Atherosclerose, UR545 INSERM, Institut Pasteur de Lille, Lille, Fr.

SOURCE: Gastroenterology (2003), 125(2), 544-555
CODEN: GASTAB; ISSN: 0016-5085

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

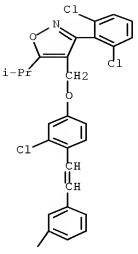
AB Background & Aims: Increased serum triglyceride levels constitute a risk factor for coronary heart disease. Apolipoprotein CIII (Apo CIII) is a determinant of serum triglyceride metabolism In this study, we investigated whether activators of the nuclear farnesoid X receptor (FXR) modulate Apo CIII gene expression. Methods: The influence of bile acids and synthetic FXR activators on Apo CIII and triglyceride metabolism was studied in vivo by using FXR wild-type and FXR-deficient mice and in vitro by using human primary hepatocytes and HepG2 cells. Results: In mice, treatment with the FXR agonist taurocholic acid strongly decreased serum triglyceride levels, an effect associated with reduced Apo CIII serum and liver mRNA levels. By contrast, no change was observed in FXR-deficient mice. Incubation of human primary hepatocytes and HepG2 cells with bile acids or the nonsteroidal synthetic FXR agonist GW4064 resulted in a dose-dependent downregulation of Apo CIII gene expression. Promoter transfection expts. and mutation anal. showed that bile acid-activated FXR decrease human Apo CIII promoter activity via a neg. FXR response element located in the 14 footprint between nucleotides -739 and -704. Chromatin immunopptn. expts. showed that bile acid treatment led to binding of FXR/retinoid X receptor heterodimers to and displacement of HNF4α from this site. Bile acid treatment still repressed liver Apo CIII gene expression in hepatic HNF4α-deficient mice, suggesting an active rather than a competitive mechanism of Apo CIII repression by the FXR. Conclusions: We identified bile acid and synthetic activators of the nuclear FXR as neg. regulators of Apo CIII expression, an effect that may contribute to the triglyceride-decreasing action of FXR agonists.

IT 278779-30-9, GW4064
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesoid X receptor agonists suppress hepatic apolipoprotein CIII expression)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:237176 HCAPLUS Full-text
DOCUMENT NUMBER: 139:17879
TITLE: Differential regulation of rat and human CYP7A1 by the nuclear oxysterol receptor liver X receptor-α
AUTHOR(S): Goodwin, Bryan; Watson, Michael A.; Kim, Hwajin; Miao, Ji; Kemper, Jongsook Kim; Kliewer, Steven A.
CORPORATE SOURCE: Nuclear Receptor Discovery Research, GlaxoSmithKline Research and Development, Research Triangle Park, NC, 27709, USA
SOURCE: Molecular Endocrinology (2003), 17(3), 386-394
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In rodent liver, transcription of the gene encoding cholesterol 7α-hydroxylase (CYP7A1), which catalyzes the rate-limiting step in the classic bile acid synthetic pathway, is stimulated by the liver X receptor α (LXRα), a nuclear receptor for oxysterol metabolites of cholesterol. This feed-forward regulatory loop provides a mechanism for the elimination of excess cholesterol from the body. The authors demonstrate that in primary cultures of human hepatocytes, activation of LXRα has the opposite effect, repressing CYP7A1 expression. This repression is mediated, at least in part, through induction of the orphan nuclear receptor, short heterodimer partner (SHP), which is also induced by bile acids. The authors demonstrate that SHP is regulated directly

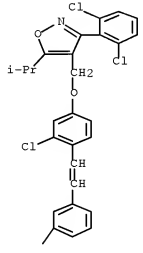
by LXRα through a DNA response element that overlaps with the previously characterized bile acid response element. The authors' data reveal a fundamental difference in the regulation of CYP7A1 in rodent and human hepatocytes and provide evidence that different species employ distinct mol. strategies to regulate cholesterol homeostasis.

IT 278779-30-9, GW4064
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(differential regulation of rat and human CYP7A1 by nuclear oxysterol receptor liver X receptor-α)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN

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|---|---|
| ACCESSION NUMBER: | 2002:615891 HCAPLUS Full-text |
| DOCUMENT NUMBER: | 137:179889 |
| TITLE: | ApoA1 promoter-derived FXR response element-based method for identifying compounds modulating reverse cholesterol transport |
| INVENTOR(S): | Staels, Bart |
| PATENT ASSIGNEE(S): | Genfit, Fr. |
| SOURCE: | PCT Int. Appl., 54 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | French |
| FAMILY ACC. NUM. COUNT: | 1 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2002063038 | A1 | 20020815 | WO 2002-FR410 | 20020204 <-- |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| FR 2820435 | A1 | 20020809 | FR 2001-1486 | 20010205 <-- |
| FR 2820435 | B1 | 20040227 | | |
| CA 2437434 | A1 | 20020815 | CA 2002-2437434 | 20020204 <-- |
| AU 2002234729 | A1 | 20020819 | AU 2002-234729 | 20020204 <-- |
| AU 2002234729 | B2 | 20070531 | | |
| EP 1358354 | A1 | 20031105 | EP 2002-701394 | 20020204 <-- |
| EP 1358354 | B1 | 20060329 | | |
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| JP 2004537272 | T | 20041216 | JP 2002-562774 | 20020204 <-- |
| CN 1568374 | A | 20050119 | CN 2002-803509 | 20020204 <-- |
| AT 321887 | T | 20060415 | AT 2002-701394 | 20020204 <-- |
| ES 2260413 | T3 | 20061101 | ES 2002-701394 | 20020204 <-- |
| US 20040115666 | A1 | 20040617 | US 2003-450257 | 20031105 <-- |
| PRIORITY APPLN. INFO.: | | | FR 2001-1486 A | 20010205 <-- |
| | | | WO 2002-FR410 W | 20020204 <-- |

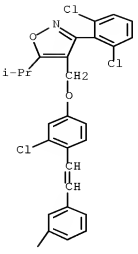
AB The invention discloses methods and compds. capable of modulating reverse cholesterol transport in a mammal and screening methods for selecting, identifying and/or characterizing compds. capable of modulating reverse cholesterol transport. The invention also discloses cells, vectors and genetic constructs used for implementing the methods, and pharmaceutical compns. for treating atherosclerosis. The inventive methods are based on the use of FXR response elements derived from the apolipoprotein A1 gene promoter.

IT 278779-30-9, GW 4064
RL: PAC (Pharmacological activity); BIOL (Biological study)
(apoA1 promoter-derived FXR response element-based method for identifying compds. modulating reverse cholesterol transport)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:677926 HCAPLUS Full-text
DOCUMENT NUMBER: 138:49877
TITLE: Lithocholic acid decreases expression of bile salt export pump through farnesoid X receptor antagonist activity
AUTHOR(S): Yu, Jinghua; Lo, Jane-L.; Huang, Li; Zhao, Annie; Metzger, Edward; Adams, Alan; Meinke, Peter T.; Wright, Samuel D.; Cui, Jisong
CORPORATE SOURCE: Department of Atherosclerosis and Endocrinology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Biological Chemistry (2002), 277(35), 31441-31447
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bile salt export pump (BSEP) is a major bile acid transporter in the liver. Mutations in BSEP result in progressive intrahepatic cholestasis, a severe liver disease that impairs bile flow and causes irreversible liver damage. BSEP is a target for inhibition and down-regulation by drugs and abnormal bile salt metabolites, and such inhibition and down-regulation may result in bile acid retention and intrahepatic cholestasis. In this study, we quant. analyzed the regulation of BSEP expression by FXR ligands in primary human hepatocytes and HepG2 cells. We demonstrate that BSEP expression is dramatically regulated by ligands of the nuclear receptor farnesoid X receptor (FXR). Both the endogenous FXR agonist chenodeoxycholate (CDCA) and synthetic

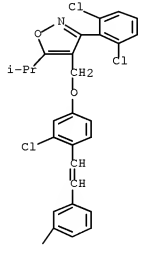
FXR ligand GW4064 effectively increased BSEP mRNA in both cell types. This up-regulation was readily detectable at as early as 3 h, and the ligand potency for BSEP regulation correlates with the intrinsic activity on FXR. These results suggest BSEP as a direct target of FXR and support the recent report that the BSEP promoter is transactivated by FXR. In contrast to CDCA and GW4064, lithocholate (LCA), a hydrophobic bile acid and a potent inducer of cholestasis, strongly decreased BSEP expression. Previous studies did not identify LCA as an FXR antagonist ligand in cells, but we show here that LCA is an FXR antagonist with partial agonist activity in cells. In an in vitro coactivator association assay, LCA decreased CDCA- and GW4064-induced FXR activation with an IC50 of 1 μM. In HepG2 cells, LCA also effectively antagonized GW4064-enhanced FXR transactivation. These data suggest that the toxic and cholestat effect of LCA in animals may result from its down-regulation of BSEP through FXR. Taken together, these observations indicate that FXR plays an important role in BSEP gene expression and that FXR ligands may be potential therapeutic drugs for intrahepatic cholestasis.

IT 278779-30-9, GW4064
RL: BSU (Biological study, unclassified); BIOL (Biological study) (endogenous FXR agonist chenodeoxycholate and synthetic FXR ligand GW4064 effectively increases BSEP (bile salt export pump) mRNA in primary human hepatocytes and HepG2 cells)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 18 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN
ACCESSION NUMBER: 2002:262042 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200262042
TITLE: Bile acid-activated nuclear receptor FXR suppresses apolipoprotein A-I transcription via a negative FXR response element.
AUTHOR(S): Claudel, Thierry; Sturm, Ekkehard; Duez, Helene; Torra, Ines Pineda; Sirvent, Audrey; Kosykh, Vladimir; Fruchart, Jean-Charles; Dallongeville, Jean; Hum, Dean W.; Kuipers, Folkert; Staels, Bart [Reprint author]
CORPORATE SOURCE: Unite de Recherche 545, Institut National de la Sante et de la Recherche Medicale, Institut Pasteur de Lille, 1 Rue du Professor, Calmette, 59019, Lille, France Bart.Staels@pasteur-lille.fr
SOURCE: Journal of Clinical Investigation, (April, 2002) Vol. 109, No. 7, pp. 961-971. print. CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002

AB Serum levels of HDL are inversely correlated with the risk of coronary heart disease. The anti-atherogenic effect of HDL is partially mediated by its major protein constituent apoA-I. In this study, we identify bile acids that are activators of the nuclear receptor farnesoid X receptor (FXR) as negative regulators of human apoA-I expression. Intrahepatocellular accumulation of bile acids, as seen in patients with progressive familial intrahepatic cholestasis and biliary atresia, was associated with diminished apoA-I serum levels. In human apoA-I transgenic mice, treatment with the FXR agonist taurocholic acid strongly decreased serum concentrations and liver mRNA levels of human apoA-I, which was associated with reduced serum HDL levels. Incubation of human primary hepatocytes and hepatoblastoma HepG2 cells with bile acids resulted in a dose-dependent downregulation of apoA-I expression. Promoter mutation analysis and gel-shift experiments in HepG2 cells demonstrated that bile acid-activated FXR decreases human apoA-I promoter activity by a negative FXR response element mapped to the C site. FXR bound this site and repressed transcription in a manner independent of retinoid X receptor. The nonsteroidal synthetic FXR agonist GW4064 likewise decreased apoA-I mRNA levels and promoter activity in HepG2 cells.

L21 ANSWER 19 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:626564 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200626564
TITLE: The protective effect of GW4064 on bile duct ligation-induced hepatotoxicity in rats: Role of activated FXR.
AUTHOR(S): Liu, Yaping [Reprint author]; Numerick, Mary Jo [Reprint author]; Dennis, Steve [Reprint author]; Binz, Jane [Reprint author]; Goodwin, Bryan [Reprint author]; Jones, Stacey A. [Reprint author]
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, USA
SOURCE: Hepatology, (October, 2002) Vol. 36, No. 4 Part 2, pp. 339A. print.
Meeting Info.: 53rd Annual Meeting on the Liver. BOSTON, MA, USA. November 01-05, 2002.
CODEN: HPTLD9. ISSN: 0270-9139.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2002
Last Updated on STN: 12 Dec 2002

L21 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:729132 HCAPLUS Full-text
DOCUMENT NUMBER: 136:18310
TITLE: Farnesoid X-activated receptor induces apolipoprotein C-II transcription: a molecular mechanism linking plasma triglyceride levels to bile acids
AUTHOR(S): Kast, Heidi Rachelle; Nguyen, Catherine M.; Sinal, Christopher J.; Jones, Stacey A.; Laffitte, Bryan A.; Reue, Karen; Gonzalez, Frank J.; Willson, Timothy M.; Edwards, Peter A.
CORPORATE SOURCE: Departments of Biological Chemistry and Medicine, University of California, Los Angeles, CA, 90095, USA
SOURCE: Molecular Endocrinology (2001), 15(10), 1720-1728
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

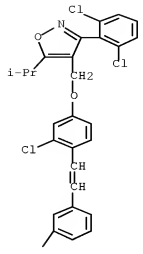
AB The farnesoid X-activated receptor (FXR; NR1H4), a member of the nuclear hormone receptor superfamily, induces gene expression in response to several bile acids, including chenodeoxycholic acid. Here the authors used suppression subtractive hybridization to identify apolipoprotein C-II (apoC-II) as an FXR target gene. Retroviral expression of FXR in HepG2 cells results in induction of the mRNA encoding apoC-II in response to several FXR ligands. EMSAs demonstrate that recombinant FXR and RXR bind to two FXR response elements that are contained within two important distal enhancer elements (hepatic control regions) that lie 11 kb and 22 kb upstream of the transcription start site of the apoC-II gene. A luciferase reporter gene containing the hepatic control region or two copies of the wild-type FXR response element was activated when FXR-containing cells were treated with FXR ligands. In addition, the authors report that hepatic expression of both apoC-II and phospholipid transfer protein mRNAs increases when mice are fed diets supplemented with cholic acid, an FXR ligand, and this induction is attenuated in FXR null mice. Finally, the authors observed decreased plasma triglyceride levels in mice fed cholic acid- containing diets. These results identify a mechanism whereby FXR and its ligands lower plasma triglyceride levels. These findings may have important implications in the clin. management of hyperlipidemias.

IT 278779-30-9, GW 4064
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(farnesoid X-activated receptor induces apolipoprotein C-II transcription in HepG2 cells in relation to mol. mechanism linking plasma triglyceride levels to bile acids)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 21 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:522315 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100522315
TITLE: Chemical genomics: Functional analysis of orphan nuclear receptors in the regulation of bile acid metabolism.
AUTHOR(S): Willson, Timothy M. [Reprint author]; Jones, Stacey A.; Moore, John T.; Kliewer, Steven A.
CORPORATE SOURCE: GlaxoSmithKline, Five Moore Drive, Research Triangle Park, NTH-M1421, Raleigh, NC, 27709-3398, USA tmw20653@gsk.com
SOURCE: Medicinal Research Reviews, (November, 2001) Vol. 21, No. 6, pp. 513-522. print. CODEN: MRREDD. ISSN: 0198-6325.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2001
Last Updated on STN: 25 Feb 2002

L21 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:441628 HCAPLUS Full-text
DOCUMENT NUMBER: 133:68969
TITLE: Assays for ligands for nuclear receptors using peptide sequences
INVENTOR(S): Blanchard, Steven Gerard; Kliewer, Anthony; Lehmann, Jurgen; Parks, Derek J.; Stimmel, Julie Beth; Willson, Timothy Mark

PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| JP 2002532729 | T | 20021002 | JP 2000-589188 | 19991222 <-- |
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| MX 2001006289 | A | 20020208 | MX 2001-6289 | 20010619 <-- |
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| US 6984650 | B2 | 20060110 | | |

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| | US 2001-868397 | A1 | 20010618 <-- |

OTHER SOURCE(S): MARPAT 133:68969

AB The present invention provides a method of identifying compds. for the treatment of diseases or disorders modulated by farnesoid X receptor (FXR), comprising the step of determining whether the compound interacts directly with FXR, wherein a compound that interacts directly with FXR is a compound for the treatment. A generic approach to assay development for nuclear receptors is presented, using purified ligand binding domains. The concept of generic assay development is extended to develop in vitro assays that detect ligand binding by monitoring ligand-induced changes in receptor heterodimerization. This approach is demonstrated using both scintillation proximity and homogeneous time-resolved fluorimetry (HTRF). Another aspect of the invention is a nuclear receptor peptide assay for identifying ligands. This assay utilizes fluorescence resonance energy transfer (FRET) and can be used to test whether putative ligands bind to FXR. The FRET assay is based upon the principle that ligands induce conformational changes in nuclear receptors that facilitate interactions with coactivator proteins required for transcriptional activation. Binding of the FXR nuclear receptor can result in the alteration of expression of various genes that FXR aids in regulating, including genes involved in lipid absorption and digestion in the small intestine and lipid homeostasis in liver. FXR often functions as a heterodimer with the RXR receptor. The inventive method includes using this technol. to affect bile acid and cholesterol homeostasis such that, ultimately, cholesterol and lipid levels can be modified and in treating diseases in a mammal, including human, in which regulation of bile acid, cholesterol and lipid levels is important. For example, GW4064 (prepared in a yield of 98%) was given to Fischer rats at a dose of 30 mg/kg for 7 days. At the and of study, serum triglyceride levels were decreased by 26% compared to a vehicle-treated controls. Nearly 20 genes were identified in the intestine that were regulated >1.5-fold by GW4064. The expression of roughly half of these genes was decreased by GW4064 treatment. All of these down-regulated

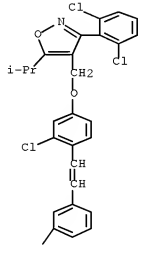
genes are involved in either lipid absorption or proteolysis, including lipases, proteases, and a colipase.

IT 278779-30-9P, GW 4064
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(identification of nuclear receptor ligands for treatment of diseases affected by cholesterol, triglycerides and bile acid levels)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

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SEARCH HISTORY

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                OR 9046-27-9/BI)

     FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 08 APR 2009
L10           1 SEA ABB=ON  L8 AND L9

     FILE 'REGISTRY' ENTERED AT 16:56:06 ON 08 APR 2009
L11           1 SEA ABB=ON  278779-30-9/RN

     FILE 'HCAPLUS' ENTERED AT 16:56:39 ON 08 APR 2009
L12          56 SEA ABB=ON  L11
L13           5 SEA ABB=ON  L12 AND (?LIVER? OR ?HEPATIC?)(4A)?FIBROSIS?

     FILE 'USPATFULL' ENTERED AT 16:57:18 ON 08 APR 2009
L14           4 SEA ABB=ON  L12 AND (?LIVER?/BI,IT,ST,CC OR ?HEPATIC?/BI,IT,ST,
                CC)(4A)?FIBROSIS?/BI,IT,ST,CC

     FILE 'HCAPLUS, USPATFULL' ENTERED AT 16:57:33 ON 08 APR 2009
L15           9 DUP REMOV L13 L14 (0 DUPLICATES REMOVED)
L16           0 SEA ABB=ON  L15 AND (PRD<20030926 OR PD<20030926)
L17          46 SEA ABB=ON  L12 AND ?LIVER?
L18          19 SEA ABB=ON  L17 AND (PRD<20030926 OR PD<20030926)

     FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 17:02:50 ON 08 APR 2009
L19           5 SEA ABB=ON  L18
L20           5 DUP REMOV L19 (0 DUPLICATES REMOVED)
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FILE 'HCAPLUS, USPATFULL, BIOSIS' ENTERED AT 17:03:37 ON 08 APR 2009
L21 22 DUP REMOV L18 L20 (2 DUPLICATES REMOVED)

FILE HOME

FILE HCAPLUS



FILE COVERS 1907 - 8 Apr 2009 VOL 150 ISS 15
FILE LAST UPDATED: 7 Apr 2009 (20090407/ED)

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 7 APR 2009 HIGHEST RN 1132879-07-2
DICTIONARY FILE UPDATES: 7 APR 2009 HIGHEST RN 1132879-07-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 7 Apr 2009 (20090407/PD)
FILE LAST UPDATED: 7 Apr 2009 (20090407/ED)
HIGHEST GRANTED PATENT NUMBER: US7516497
HIGHEST APPLICATION PUBLICATION NUMBER: US20090089907
CA INDEXING IS CURRENT THROUGH 7 Apr 2009 (20090407/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 7 Apr 2009 (20090407/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2008
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2008

USPATFULL now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

FILE MEDLINE
FILE LAST UPDATED: 7 Apr 2009 (20090407/UP). FILE COVERS 1949 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2009 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Libra of Medicine (NLM). Additional information is available at

http://www.nlm.nih.gov/pubs/techbull/nd08/nd08_medline_data_changes_2009.

On February 21, 2009, MEDLINE was reloaded. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 1 April 2009 (20090401/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE
FILE COVERS 1974 TO 8 Apr 2009 (20090408/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE DRUGU
FILE LAST UPDATED: 8 APR 2009 <20090408/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<